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The Threshold Force for Membrane Tether Formation Depends Strongly on Loading Rate
Daniel Stark, Thomas Killian, **Robert Raphael**.
Rice University, Houston, TX, USA.
Tethers are thin tubes of lipids (~20-200 nm in diameter) that form when membranes are subjected to a point force. Tether dynamics are important to a myriad of biological processes including white blood cell adhesion and transport of intracellular material between neighboring cells. To understand the dynamics of tether formation more fully, we investigated the dependence of the force needed to create a tether on the rate of force change (loading rate). To conduct these experiments, a microfabricated magnetic force transducer was used to generate well-controlled and localized magnetic force profiles. Tethers were formed off the surface of microaspirated giant unilamellar vesicles (GUVs) attached to magnetic beads. We discovered a strong correlation between the threshold force of tether formation and the applied force ramp, with the force changing from $<$10 pN at low loading rates to ~50 pN at high loading rates. At slow loading rates, the threshold force changes weakly with ln (loading rate), while at high loading rates a steeper dependence is observed. The experimental data can be fit to a energetic model based on Kramer's theory, similar to models used to describe membrane rupture. The model predits that tether formation involves passage over two energy barriers and enbales characterization of the characteristic forces and timescales associated with these barriers. This new tool for dynamic studies of membrane mechanics may further be extended to study how tethers form off of flowing cells or how phase regimes, induced by the presence of cholesterol, influence membrane dynamics.

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Solid-State ^{2}H NMR Reveals Changes in Membrane Flexibility Due to Osmotic Pressure
K.J. Mallikarjunaiah[1], Michael F. Brown[1,2].
[1]Department of Chemistry and Biochemistry, University of Arizona, Tucson, AZ, USA, [2]Department of Physics, University of Arizona, Tucson, AZ, USA.
Cellular membrane properties are sensitive to pressure, temperature, and dehydration as well as lipid composition, which can affect function through non-specific lipid-protein interactions [1]. Functional lipid rafts in cellular membranes may correspond to detergent-resistant domains due to the presence of cholesterol. Changes in swelling and stiffening of pure lipid bilayers in the liquid-crystalline phase have been observed [2-4] with addition of detergent and cholesterol. Here we show how structure and associated dynamics of mixed-lipid bilayers are affected by osmotic pressure. Determinations of area per lipid and motional parameters of DMPC membranes in the presence of detergent ($C_{12}E_8$) or cholesterol utilize ^{2}H NMR together with a mean-torque model for interpreting acyl-chain order parameters (S_{CD}) [5]. Swelling by addition of detergent is due to enhanced membrane flexibility, and is counteracted by applying osmotic pressure to the lipid dispersion. By contrast, reduced swelling of multilamellar dispersions due to the stiffening action of cholesterol is reinforced by osmotic pressure. In both cases the membrane area compressibility modulus K_a is calculated from S_{CD} order parameters. We propose that apparent K_a values differ with osmotic pressure for both systems due to changes in the hierarchy of forces and motions. Calculation of the bilayer bending rigidity and the area elastic modulus provides a basis for molecular dynamics simulations of membrane deformations at the atomistic and mesoscopic levels. Osmotic pressure-induced deformation of membranes reveals how lipid-protein interactions can play key roles in biological functions of pressure-sensitive proteins and channels. [1] K.J. Mallikarjunaiah *et al*. (2011) *BJ* **100**, 98-107 [2] M.F. Brown *et al*. (2002) *JACS* **124**, 8471-8484. [3] D. Otten *et al*. (2000) *JPC* **104**, 12119-12129. [4] G.V. Martinez *et al*. (2002) *PRE* **66**, 050902. [5] H.I. Petrache *et al*. (2000) *BJ* **79**, 3172-3192.

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Inhibition of the Peroxidation of Liposomal Lipids by Uric Acid Requires Tocopherol
Dov A. Lichtenberg, Dorit Samocha-Bonet, Ilya Pinchuk.
Tel Aviv University, Tel Aviv, Israel.
Urate is the major water-soluble low molecular weight antioxidants in serum, contributing about 50% to the antioxidative potential of the serum. Unexpectedly, both urate, as well as the other major antioxidant ascorbate, promote the copper-induced peroxidation of liposomal PUFA. In a previous study it has been shown that ascorbate inhibits copper-induced oxidation of liposomal lipids when the liposomes contain Tocopherol, whereas urate does not. In an attempt to explain these findings we studied the temporal order of events, by monitoring continuously and simultaneously the time-course of formation of oxidation products and the consumption of the various components of the system. The resultant kinetic profiles show that: 1. Both water-soluble antioxidants slightly inhibit the oxidation of tocopherol; 2. Ascorbate becomes oxidized very rapidly (much faster than tocopherol), whereas urate and tocopherol become oxidized simultaneously. 3. In the presence of tocopherol, both urate and ascorbate inhibit copper-induced peroxidation of PUFA. 4. AAPH-induced peroxidation of liposomal PUFA is inhibited by both urate and ascorbate, independent of the presence of tocopherol. Our interpretation of these results contribute to the understanding of the complex, interdependent dependence of the susceptibility of aggregated (unlike soluble) lipids on all the water-soluble antioxidants. This is particularly important for evaluation of the oxidizability of serum lipids when the serum contains excess urate, as in the case of insulin-resistant and obese subjects.

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From Thermodynamic States to Biological Function by Einstein's Approach to Statistical Physics
Matthias F. Schneider[1], Stefan Nuschele[2], Shamit Shrivastava[1], Christian Fillafer[1], Bernhard Fichtl[1], Israel Silman[3], Konrad Kaufmann[4].
[1]Biological Physics Group - Boston University, Boston, MA, USA, [2]Biological Physics Group - Universiaet Augsburg, Augsburg, Germany, [3]Department of Neurobiology and The Israel Structural Proteomics Center, Weizmann Institute of Science, Rehovot, Israel, [4]Max-Planck-Institute for biophysical Chemistry, Göttingen, Germany.
Einstein founded statistical physics on an important generalization of the Boltzmann principle: Einstein's reversion, where not the model but the law of entropy is placed first. The advantage is that it assures the 2nd Law and requires no model assumptions. In particular, the existence of a complete molecular mechanism is not necessary. However, if the empirical behavior of a system is known, the entropy and the corresponding probability of the thermodynamic states can be directly derived. With his approach Einstein successfully explained Brownian motion, wave-particle dualism, quantum transitions as well as the Bose-Einstein condensation.
Impossible to find in any textbook, we outline Einstein's approach and apply it to soft interfaces. The introduction of their proper entropy potential, its first, and its second derivatives predicts interfacial nonequilibrium excitation, propagation, and fluctuations, respectively. Experimental observations of the phenomenology of the membrane susceptibilities allow quantitative predictions. The propagation of waves as well as the existence of channel-like current fluctuations are experimentally confirmed and compared to measurements on living systems.
Finally, we present experiments that confirm Einstein's approach to the interfacial reaction coordinate. Here the phenomenology of the system is derived from a proper entropy law even though hidden from direct observation. Not structure of molecules but entropy of the aqueous interfaces turns out to be the origin of catalysis and the associated surprising increase in reaction rate. Simultaneous specificity and activity appears now predictable and no more paradox. The theory derived from K.K. in 1999 is briefly outlined and confirmed in experiments on Acetylcholinesterases incorporated in lipid monolayers. Since enzyme activity is controlled from remote by these continuous layers, our results predict the ubiquitous, integrative action in biology of the excitable hydration interface.

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Polymer Mediated Interactions Between Myelin Lipid Bilayers
Xavier Banquy, Dong Woog Lee, Kai Kristianson, Jacob N. Israelachvili.
University of California, Santa Barbara, Santa Barbara, CA, USA.
The axons of the central nervous system are covered by a multi-layered membrane which provides insulation and high electric signal conductivity to the axons. Swelling of the myelin sheaths is the hallmark of many neurological degenerative diseases like multiple sclerosis. Loss of the myelin membrane involves subtle changes in the interaction forces that hold the membrane stack together. These interaction forces are believed to have more than one origin, the major one arising from the dedicated protein -myelin basic protein (MBP) - which binds to, and bridges, the cytoplasmic sides of myelin membrane via electrostatic and hydrophobic interactions. It has been shown that deimination of MBP leads to a loss of adhesion between myelin membranes and ultimately to swelling of myelin. In the present study, we explored a new strategy that makes use of structured polymers to reverse the effects of loss of adhesion between myelin membranes. By controlling the chemical composition and architecture of the polymers, our results show that it is possible to enhance the adhesion between the membranes using different types of interaction forces like electrostatic forces, depletion forces, bridging forces or combinations of them. Neutral triblock copolymers with a central hydrophobic segment present a strong affinity to the bilayers and enhance the adhesive interaction forces between the membranes via a depletion mechanism similar to hydrophilic homopolymers (like PEG). On the other hand, triblocks copolymers with two